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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/190,043	11/10/98	HOUCK J	47.653.2

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EXAMINER	
BORIN, M	
ART UNIT	**PAPER NUMBER**
1631	14

DATE MAILED: 08/14/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/190,043	Applicant(s) Houck et al.
	Examiner M. Borin	Group Art Unit 1631

☒ Responsive to communication(s) filed on *Jun 12, 2000* .

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-20* is/are pending in the application.

Of the above, claim(s) *4-20* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-3* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Status of Claims

1. Amendment filed 06/12/00 is acknowledged. Claim 1 is amended. Claims 1-20 are pending. Claims 4-20 remain withdrawn from consideration. Applicant informs that the non-elected claims 4-20 will be canceled.

2. Rejection under 35 U.S.C. § 112, first paragraph, is withdrawn in view of applicants arguments.

Claim Rejections - 35 U.S.C. § 103.

3. Applicants arguments with respect to rejection made under 35 U.S.C. 103 have been considered but are not deemed to be convincing for the reasons stated below.

4. The rejection of claims 1-2 is maintained under 35 U.S.C. 103(a) as obvious over Gleisner (Inflammation, 5, 13-17, 1981) in view of Oxford Dictionary of Biochemistry and Molecular Biology (1981) and Casale and Dimitrascu, and further in view of Kermode.

The references of Ferry and Anderson are not used in the rejection because the scope of the claims is now limited to one peptide, f-Met-Leu-Phe-Phe.

The instant claims are drawn to method for treating allergy reaction by formyl Met peptides having formula f-Met-Leu-X.

Gleisner teaches that formyl Met peptides are capable of reducing effect of other pro-inflammatory agents (such as 48/80, anti-rat IgE, etc) in that they inhibit the evoked mast cell degranulation and histamine release. Particular examples of the formyl Met peptides are f-Met-Phe, f-Met-Leu-Phe. The study concludes that the formyl Met peptides described in the reference as well as their structural analogs can be a useful addition to the existing antihistaminic drugs. See p. 16, end. It is well known that antihistamine drugs are used in the treatment of allergy reactions. See, e.g., Oxford Dictionary of Biochemistry and Molecular Biology, 1997, p. 43. It is well known as well that mast cells are the most important cells in the development of allergenic response. References of Dumitrascu and Casale are provided as an example. Therefore, it would be obvious to use formyl Met peptides in the treatment of allergy reactions.

In regard to particular formyl Met peptides, a variety of preferred species of formyl Met peptides is known in the prior art. Thus Kermode (reference AE) discloses that formyl Met peptides, such as f-Met-Leu-Phe, f-Met-Leu-Phe-Phe and f-Nle-Leu-Phe-Tyr as functional equivalents. In particular, f-Met-Leu-Phe-Phe (i.e., the peptide used in the instant method) is one of the most potent formyl Met peptides analogs. See p.276, first paragraph; Tables 1,2; Fig.2;p. 719. Therefore, it would have been *prima facie* obvious to use the peptide f-Met-Leu-Phe-Phe as anti-allergic agent because Gleisner teaches that formyl-Met peptides can reduce anti-histamine release caused by other inflammatory agent (i.e., to cause anti-allergic effect) and Kermode teaches that f-Met-Leu-Phe-Phe is one of the most potent formyl-Met peptides.

Response to arguments

On the onset, Applicants again, have traversed the primary and the secondary references pointing to the differences between the claims and the disclosure in each reference. Applicant is repeatedly reminded that the rejection is under 35 U.S.C. 103 and that unobviousness cannot be established by attacking the references individually when the rejection is based on the combination of the references. It has been well established that the test for combining references is not what individual references themselves suggest but what the combination of disclosures taken as a whole would suggest to one of ordinary skill in the art. *In re McLaughlin,* 170 USPQ 209 (CCPA 1970).

Applicant argues, first, that different structurally similar formyl-Met peptides will not have the same effect, and illustrates it citing examples of dipeptides f-Met-Phe or Met-Phe (p. 3 of the response). The instant claim 1 is now amended to read only on one peptide, tetrapeptide f-Met-Leu-Phe-Phe. This particular peptide is described in Kermode as one of the most potent f-Met peptides (see the rejection above). In discussing Kermode reference, applicant makes contradictory statements, first providing citation from the reference showing that f-Met-Leu-Phe-Phe is indeed the most potent formyl peptide, but that the low-affinity binding varies to a greater extent than high affinity binding, and immediately following with a citation showing that the low affinity binding is of now relevance to a formyl peptide's potency to stimulate degranulation. From this discussion applicant draws conclusion that different formyl peptides are not functionally equivalent (See p. 4 of the response).

Further, applicant argues that the applicability of formyl peptides to treat allergy reaction is discovered in the instant invention. Once again, applicants attention is pointed at Gleisner reference

which teaches that formyl Met peptides are capable of reducing effect of other pro-inflammatory agents (such as 48/80, anti-rat IgE, etc) in that they inhibit the evoked mast cell degranulation and histamine release.

Applicant then discusses the Clagett declaration which presumably demonstrates unexpected anti-inflammatory effect of f-Met-Leu-Phe-Phe. Note, however, the essential difference in the effect of a biological mediator (such as chemotactic f-Met peptide) when it is used alone as compared to its use in the presence of another pro-inflammatory agent. Cellular response to f-Met peptides (which can be described as inflammatory response) is the same type of protective reaction which mediates response of the organism to a foreign infection. It is well known in the art that biological mediators such as chemotactic factors stimulate the migration of neutrophils from circulation into sites of infection or tissue damage. These mediators are also believed to increase cell adhesion to injured sites and to activate neutrophils to release toxic agents such as oxygen metabolites and proteases. Thus, in the presence of a provoked infection the response caused by f-Met peptides have protective, anti-inflammatory function. An example of an agent which, similarly to f-met peptides, can be either pro- or anti-inflammatory was given in the previous Office action: Effects of colony-stimulating factor (CSF) are similar to those of formyl peptides. See, e.g., Beaulieu et al., Wright et al. CSF is one of the leading mediators of inflammation. See, e.g., al-Janadi et al. At the same time CSF is being used to treat inflammation. See, e.g., Burak et al. (The references have been cited and their copies have been enclosed in co-pending case 09/189130).

Characteristically, in the Declaration filed 06/12/00 the effect of the f-Met-Leu-Phe-Phe (fMLFF) is demonstrated only as inhibitor of inflammatory effect caused by another f-Met peptide, fMLP. The absence in the Declaration of showing of the effect of fMLPP alone is not surprising because Kermode shows (Table 2) that fMLPP (the peptide of the claimed composition) is more potent chemotactic agent and stimulator of neutrophil degranulation than the fMLP (the peptide used as "pro-inflammatory" agent). One would expect that fMLPP, alone, would be at least as "pro-inflammatory" as fMLP. There is no proper comparison in effects of the two formyl peptides used in the Declaration to demonstrate unexpected results.

5. Claim 3 remains rejected under 35 U.S.C.103(a) for the reasons of record because the rejection of claims 1,2 is maintained as discussed above.

Conclusion.

6. No claims are allowed

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be

calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (703) 305-4506. Dr. Borin can normally be reached between the hours of 8:30 A.M. to 5:00 P.M. EST Monday to Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Mr. Michael Woodward, can be reached on (703) 308-4028. The fax telephone number for this group is (703) 305-3014.

Any inquiry of a general nature or relating the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

9. The Art Unit of your application in the PTO has changed. To aid any papers for this application, all further correspondent should be directed to Art Unit 1631.

August 7, 2000

mlb

MICHAEL BORIN, PH.D.
PATENT EXAMINER